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Is Platelet Rich Plasma Injection an Effective Treatment for Hair Loss in Androgenic Alopecia and Alopecia Areata?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies

Philadelphia College of Osteopathic Medicine

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Abstract

Objective: The objective of this selective EBM review is to determine whether or not Platelet Rich Plasma is efficacious in regrowth of hair in both androgenic alopecia and alopecia areata.

Study Design: Review of two blinded randomized controlled trials and one prospective cohort study. Populations studied were Adults over 18 with hair loss. All articles published in peer-reviewed journals in English.

Data Source: 3 articles found via PubMed and NCBI

Outcomes Measured: One prospective cohort study, and two randomized control trials evaluating hair regrowth after PRP scalp injections. Outcomes were reported by patient satisfaction, mean hair increase and hair regrowth in hair loss areas.

Results: Gentile (2015) enrolled 23 patients with androgenic alopecia, with 3 withdrawals. After PRP injection a mean increase in total hair density of 45.9 hairs per cm² compared with baseline was observed at 3 months. Ginki (2014) enrolled 22 volunteers with androgenic alopecia, with 2 withdrawals. Hair densities were reported at monthly intervals with the highest reported at 4 months: 170.70 plus or minus 37.81 hairs. Trink (2013) enrolled 45 patients with alopecia areata, with no withdrawals. 60 percent of the patients in the PRP group had complete remission of alopecia as compared to placebo.

Conclusion: PRP injection for androgenetic alopecia and alopecia areata is a simple, safe and cost effective treatment for hair loss or thinning.

Key words: Hair loss, PRP injection, platelet rich plasma, PRP and hair growth.

Introduction

Androgenic alopecia (AGA) and alopecia areata (AA) are common hair loss disorders affecting adult populations worldwide. Alopecia areata is an autoimmune cause of hair loss and most common type in younger populations. Androgenic alopecia, also known as male pattern hair loss (MPHL) is the most common form of alopecia and affects up to 80% of white men and 40% of women.¹ With such a strong prevalence, Physician Assistants in any field, certainly dermatology, can expect to counsel patients on alopecia throughout their careers.

The etiology of male pattern hair loss is androgen-dependent, and a genetically determined trait. Dihydroxytestosterone (DHT) synthesized from testosterone by an enzyme called 5alpha-reductase is thought to be the principal agent for MPHL.⁴ DHT binds preferentially to hair follicles, as compared to testosterone. Males with AGA have consistent higher levels of DHT and 5alpha-reductase as compared to non-balding counterparts.⁴

Female pattern hair loss (FPHL) (or female androgenetic alopecia) is believed to be the same entity.⁴ However, the requirement of androgens is less clear-cut than in men and the distribution of hair loss is generally different.⁴ In both men and women normal hair follicles follow a life cycle where the hair follicle undergoes a phase of rapid growth (anagen) to a resting period (telogen). In both men and women, AGA is characterized by an ongoing decline in the duration of anagen, and increase in the duration of telogen and miniaturization of scalp hair follicles.⁴

Alopecia areata (AA) is a common autoimmune condition, causing inflammation induced hair loss. According to the National Alopecia Areata Foundation Over 6.6 million people in the United States and 147 million worldwide have or will develop alopecia areata at some point in

their lives. It is a common cause of abrupt-onset hair loss, with both sexes affected equally.

Clinically presents with well-demarcated round or oval bald spots on the scalp or other parts of the body.⁴ Although it may occur at any age, alopecia areata is the most common form of alopecia seen in children. Currently no FDA approved treatment exists.³

There is no exact number for health care visits or cost on health care system related to treating alopecia. With such a variability in treatment options and the cosmetic nature of the disease, figures reported are not consistent. Currently two FDA approved pharmaceuticals exist for androgenic alopecia: Topical Minoxidil and oral finasteride. Oral finasteride is a 5alpha-reductase inhibitor which prevents conversion of testosterone to DHT. The side effect profile includes decreases sex drive or ability.⁶ Minoxidil, a piperidinopyrimidine derivative, was noted to cause hypertrichosis when administered orally as an antihypertensive.⁴ It is now used as a 2% and a 5% topical treatment in a lotion or foam preparation.⁴ The mechanism of action is not fully understood. Clinical trials in only the vertex region of the scalp have shown regrowth in up 30%–45% of patients.⁴ Some patients experience an increased shedding in the first 4–6 weeks of application.⁴ Once started Minoxidil has to be taken indefinitely, with discontinuation any potential hair regrowth will return to baseline.

Hair Restoration Surgery stands as the most definitive treatment. The most advanced method is Follicular Unit Transplant (FUE). With this procedure, hair follicles are extracted from the occipital and parietal region. Hair from this region is generally resistant to androgenic alopecia and placed in desired areas, usually from the frontal to crown regions. Hair transplant prices vary by region and clinic, but the range is typically from \$2 to \$10 per graft, with \$4-5 per graft being the average.⁵ The total cost can range anywhere from \$2,500 to \$20,000.⁵ Transplant is classically permanent, however pattern hair loss of non- transplanted hair will continue. With

the invasive nature of the procedure and high cost there continues to be room for advancement in treatment of androgenic alopecia and alopecia areata.

Platelet Rich Plasma (PRP) has emerged as a new treatment modality in regenerative plastic surgery and preliminary evidence suggests it might have a beneficial role in hair regrowth.. Platelet Rich Plasma is defined as an autologous concentration of plasma with a greater count of platelets than that of whole blood.² Using the patient's own blood, PRP is extracted. It's action depends on the released growth factors from platelets. It has been investigated and used in numerous fields of medicine. Proponents of PRP technology suggest that its benefits include hard and soft tissue wound healing, and it is used in this manner in orthopedics, dermatology, maxillofacial surgery and plastic surgery.^{1, 2} PRP injection pricing varies by region with average price around 600-800 US Dollars per treatment.⁴

Currently PRP is being investigated for hair regrowth with limited published data available. No published trials exists for using PRP in treatment alopecia areata. As a mechanism for hair growth Activated PRP seems to promote numerous growth factors. These include activation of transforming growth factor, platelet derived growth factor, vascular endothelial growth factor, epidermal growth factor and insulin like growth factor.¹ It is proposed that these factors released from platelets act on the stem cells at the base of the follicle to promote growth and revascularization.² This paper will evaluate these preliminary findings in both alopecia areata and androgenic alopecia.

Objective

The objective of the selective EBM review is to determine whether or not Platelet Rich Plasma Injection is Efficacious in Treatment of Hair Loss in Androgenic Alopecia and Alopecia Areata?

Methods

In selecting the studies for this review, the author applied the following criteria. The enrolled populations had to be at least 18 years old with hair loss of non-traumatic etiology of either androgenic alopecia or alopecia areata. Inclusion: Adults over 18 year old with hair loss, Patient suitable for PRP injection from a surgical point of view. This entailed scalp free of any skin condition such as keloids, cellulitis, any break in skin integrity or hematologic pathology rendering scalp injection high risk. The alopecia areata group had to have recurrent disease of at least 2 years duration. Exclusion criteria: Any medical or drug related hair loss. Platelet disorder, thrombocytopenia, bone marrow aplasia, uncompensated diabetes, sepsis, cancer, antiaggregating therapy, systemic or topical treatment for male pattern hair loss in past 6 months for Gkini, and 12 months for Gentile. Topical drugs in exclusion criteria included Minoxidil, prostaglandin, analogs, retinoids, and corticosteroids. (Please see Table 1 for details of inclusion/exclusion criteria and patient demographics)

Table 1: Demographics and Characteristics of included studies

Study	Type	#Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Gentile ¹ (2015)	RCT	23	19-63	Age 19-63, male pattern hair loss Stage IIa-Stage IV according to the Norwood-	Platelet disorder, thrombocytopenia antiaggregating therapy, systemic treatment for male pattern hair loss in	3	PRP

				Hamilton classification, suitable for PRP injection.	past 12 months, bone marrow aplasia, uncompensated diabetes, sepsis, cancer, immune compromised and keloids.		
Gkini ² (2014)	Prospective Cohort Study	22	24-72	Volunteers over 18 years of age with diagnosed androgenic alopecia, Had not received any topical or systemic treatment for their hair loss during the last 6 months.	Present history of immunosuppression (malignancy, chemotherapy, steroid therapy), dermatological disease affecting the scalp, autoimmune disorders, hematologic disorders, platelet dysfunction syndrome and on anticoagulation therapy, Aspirin or NSAIDs discontinued use 7 days before treatment/ Any other cause of hair loss.	2	PRP
Trink ³ (2013)	RCT	45	>18	45 male and female otherwise healthy patients with chronic, recurring alopecia areata, of at least 2 years duration. Having between four and 6 symmetrically distributed patches of hair loss.	Any medical conditions or other scalp or hair disease	0	PRP

Search Strategy

All studies had to be published in peer reviewed journals in English, no earlier than 2013.

The author searched the articles via PubMed, NCBI, and Medline. Key words: hair loss, PRP injection, PRP and hair growth, platelet rich plasma. Articles were selected based on relevancy and if they included patients oriented outcomes, i.e. (hair regrowth).

Outcomes Measured

The intervention had to be PRP scalp injection using patients own blood with the outcomes measured being hair regrowth and mean hair increase. The three articles evaluated include one prospective cohort study, and two randomized control trials evaluating hair regrowth after PRP scalp injections. The prospective study by Trink had no comparison groups, all patients were injected treated with PRP and followed for hair regrowth. The RCT by Gentile and Gkini included a placebo and treatment group. Statistics reported or used: RRR, ARR, NNT, and P-values. How are they measured: Dermoscopic evaluation of scalp for Hair regrowth in bald spots, Patient satisfaction, Mean +/- standard deviation of hairs, mean hair increase.

Results

In all studies PRP was obtained by peripheral venous access, withdrawing and centrifuging patients' blood. Interfollicular injection of PRP was performed by experienced Physicians in each of the studies. In the study by Gentile, 23 patients were enrolled with 3 that withdrew and were not included in statistical analysis. Outcomes were measured by mean hair increase after PRP injection. All patients were evaluated at beginning of study, 2months, 6, 12, 16 and 24 months. The results of this study showed a significant increase in the mean hair count for the treatment area after 3 months (3 months vs. 0 month), with a mean increase of 33.6 hairs in the target area compared with baseline, while the control area showed a mean decrease of 3.2 hairs (control vs. treatment: $p = .0001$). Accordingly, in the treatment area, a mean increase in total hair density of 45.9 hairs per cm^2 compared with baseline was observed after 3 months, and the control area displayed a mean decrease of 3.8 hairs per cm^2 in hair density at the same time (control vs. treatment: $p = .0001$). In addition, terminal hair density improved significantly by 40.1 hairs per cm^2 in the treatment area compared with baseline, while it decreased by 5.6 hairs per

cm² in the control area of the scalp (control vs. treatment: $p = .0003$). There were no statistically significant differences in villus hair density between the study and the control area after 3 months.

In the Study by Ginki, 22 volunteers (20 men, 2 women) with androgenic alopecia were enrolled. Of the 22 patients enrolled, 2 withdrew and were not included in statistical analysis. The outcomes were measured by satisfaction questioner and mean hair increase. Hair regrowth satisfaction surveys reported a high satisfaction rate of 7.1 on a 1-10 scale. 85% of Patients of patients reported an improvement in hair quality and thickness. 65% of patients reported an increase in hair density.

Additionally mean Hair densities were reported at many time intervals of treatment. All tests were two tailed with P values less than .05. Time intervals were in months. Hair density (hair/cm²) significantly increased at T3 (154.80 ± 34.39), at T4 (170.70 ± 37.81) at T5 (156.23 ± 37.75) and at T6 (153.70 ± 39.92) ($P < 0.001$) compared to the onset of therapy (T1). The highest hair density recorded was at T4 (4 months post PRP injection).² The percent increase rate from baseline (T1) was 0.45%, 8.18%, 19.9%, 9.19% and 7.41% at T2, T3, T4, T5 and at T6, respectively.² Regarding failure rate none of the patients presented decreased hair density compared to that of baseline. One patient reported no change in hair density or growth at T3 and T4. At T5 (5 months past treatment) one patient a decrease of 1 hair/cm² in hair density comparing to that of T1. And at T6 30% of patients presented a mean decrease of 2 hair/cm².

Trink enrolled 45 patients with alopecia areata (20 men, 25 women, mean age 28 years). No patients were excluded from the study. Patient were randomized and 15 patients received placebo, 15 received PRP injection and 15 received a TrA (triamcinolone acetonide) which is a treatment option for alopecia areata not approved by the FDA. Outcomes were measured by

dermoscopic evaluation of scalp for Hair regrowth in alopecia areata bald spots. PRP Platelet Rich Plasma was found to increase hair growth significantly and to decrease hair dystrophy as compared to placebo. 60 percent of the patients in the PRP group had complete remission of alopecia as compared to placebo. A numbers needed to treat (NNT) analysis shows that a PA would need to treat 3 patients with platelet rich plasma to prevent 1 patient from having continued bald spots, compared with control.

Safety: Patients own blood was used for all three PRP injection studies. No adverse reactions or events were reported. Lidocaine was used to anesthetize the scalp so the procedure was very tolerable.

Discussion

Androgenic Alopecia remains the most common hair disorder without satisfactory treatment. Due to the shortened anagen phase and diminishing hair follicle, characteristic of AA, current therapeutic therapies target proliferation during the hair cycle. Numerous products have been proposed with only minoxidil and finasteride approved by the FDA. Minoxidil prolongs anagen phase and increases hair follicle size.² Finasteride has been shown to reduce pattern hair loss associated with increased expression of caspases and apoptosis related androgen.² However, these medications have their limitations in efficacy, compliance, and patient satisfaction. Additionally a variety of both topical and systemic side effects exist, with erectile dysfunction as an example. Hair transplant is currently the most definitive option but comes with a high cost, downtime from work and dependence on donor area for hair grafts. The search continues for new treatment option for alopecia.

Presently PRP is being investigated for hair regrowth with limited published data available. Alopecia areata is an autoimmune cause of hair loss, without any FDA approved treatment modality. Furthermore, no published trials exist for using PRP in treatment of alopecia areata. As a mechanism for hair growth Activated PRP seems to promote numerous growth factors. PRP induced activation of antiapoptotic regulators such as Bcl-2 protein and Akt-signaling, which prolongs survival of dermal papilla cells during the hair cycle.² This activation also includes transforming growth factor, platelet derived growth factor, vascular endothelial growth factor, epidermal growth factor and insulin like growth factor.¹ It is proposed that these factors released from platelets act on the stem cells at the base of the follicle to promote growth and revascularization, prolonging the anagen phase of the hair cycle.²

In summary, Gentile (2015) enrolled 23 patients with androgenic alopecia, with 3 withdrawals. After PRP injection a mean increase in total hair density of 45.9 hairs per cm² compared with baseline was observed at 3 months. Ginki (2014) enrolled 22 volunteers with androgenic alopecia, with 2 withdrawals. Hair densities were reported at monthly intervals with the highest reported at 4 months: 170.70 plus or minus 37.81 hairs. Trink (2013) enrolled 45 patients with alopecia areata, with no withdrawals. 60 percent of the patients in the PRP group had complete remission of alopecia as compared to placebo. With these combined results it is clear that Platelet Rich plasma is efficacious treatment for both androgenic alopecia and alopecia areata.

Some sources error might include lack of common reference protocol for PPR preparation and injection. For example, volumes of PRP injected varied between studies or was not specified. Different brands of equipment were used with different physicians injecting the

scalp. Time intervals of injection and frequency also varied. The degree of hair loss also varied between patients, although this would be a nearly impossible variable to control.

Conclusion

PRP injection for androgenetic alopecia and alopecia areata is a simple, safe and cost effective treatment for hair loss or thinning. The product is entirely from the patient's own blood so any adverse effects are unlikely. The results showed reasonable improvement in hair loss, however far from complete resolution of alopecia. With only a handful of peer reviewed articles on PRP injection, clinical evidence is still weak. Future studies should incorporate a much larger sample size. I think it would also be beneficial for a board of PRP super-users to define an unequivocal reference protocol. This should including explicit placement instruction for PRP injection with set volume and details on increments into the scalp.

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